

PATENT/Docket No. PC27664A
Serial No. 10/644,516

II. AMENDMENTS TO THE CLAIMS

Please amend the claims as follows:

1. (original) An article of manufacture comprising a vial having
 - (a) a first chamber that is substantially filled with a parenterally deliverable aqueous suspension that comprises (i) an aqueous medium; (ii) a drug in solid particulate form in a therapeutically effective amount suspended in the medium; and (iii) one or more wetting and/or suspending agents in an amount effective to provide controlled flocculation of the drug, at least one ingredient of the formulation being susceptible to oxidative degradation;
 - (b) a second chamber that is substantially empty but for a gaseous medium;
 - (c) a septum separating the first and second chambers and impermeable to the gaseous medium; and
 - (d) actuating means effective to bring the aqueous suspension and the gaseous medium into contact by breach of the septum such that the gaseous medium acts as an effective headspace for agitation of the formulation.
2. (original) The article of Claim 1 wherein the second chamber forms a lower compartment and the first chamber forms an upper compartment; said lower and upper compartments being separated by a constriction wherein the septum in a form of a substantially airtight and watertight plug is engaged; said upper compartment having an annular neck terminating in an open end; said neck having engaged thereon a closure structure comprising (i) a resiliently flexible stopper having a lower sealing portion seated within the neck and an upper protruding portion that projects coaxially beyond the of the neck; said stopper having a deep recess open at the base thereof and closed at the apex thereof such that the apex of the recess is in proximity to the upper surface of the protruding portion, defining a thin wall portion of the stopper that permits a sharp tip of a syringe needle to be inserted through the thin wall into the upper compartment for withdrawal of the formulation therein; and (ii) a cap assembly that incorporates said actuating means, wherein said actuating means is a means for applying hydraulic pressure via the formulation in the upper

PATENT/Docket No. PC27664A
Serial No. 10/644,516

compartment to the plug, said pressure tending to disengage the plug from the constriction, thereby pushing the plug into the lower compartment to bring the formulation into contact with the gaseous medium in the lower compartment.

3. (original) The article of Claim 2 wherein the means for applying hydraulic pressure comprises a sleeve of the cap assembly that is snugly disposed around and slidingly engaged with the protruding portion of the stopper; and wherein the sealing portion of the stopper is of larger diameter than the protruding portion and defines at the interface therewith an annular shoulder; said sleeve, adjacent to a lower end thereof, being fracturably connected to an annular gripping portion of the cap assembly; said gripping portion surrounding an radially outward projecting rim formed at the open end of the neck and having at the lower edge of the gripping portion a plurality of substantially uniformly spaced projections extending radially inward; said gripping portion comprising an annular plate that overlies the open end of the neck and circumscribes a plate opening of diameter smaller than the neck opening, such that the annular plate projects radially inward to overlap the stopper shoulder and thereby positively retain the stopper in the neck; said sleeve having, on an outer surface thereof, a plurality of parallel and substantially uniformly spaced ramps that extend axially from and converge with the sleeve toward the gripping portion and that function as a locking means for retaining the sleeve in an actuated position; said sleeve being actuatable by depression thereof to break the fracturable connection and engage with the stopper shoulder to push the stopper downward, thereby creating hydraulic pressure in the upper compartment.
4. (canceled)
5. (original) The article of Claim 1 wherein the gaseous medium is air.
6. (original) The article of Claim 1 wherein the at least one oxidative degradation susceptible ingredient present in the formulation comprises a polyoxyethylene chain.
7. (original) The article of Claim 1 wherein the at least one oxidative degradation susceptible ingredient present in the formulation is a polyoxyethylene surfactant.

PATENT/Docket No. PC27664A
Serial No. 10/644,516

8. (original) The article of Claim 7 wherein the polyoxyethylene surfactant is a polysorbate.
9. (original) The article of Claim 7 wherein the polyoxyethylene surfactant is polysorbate 80.
10. (original) The article of Claim 9 wherein the polysorbate 80 is present in an amount of about 0.1 to about 10 mg/ml.
11. (original) The article of Claim 9 wherein the polysorbate 80 is present in an amount of about 1 to about 5 mg/ml.
12. (original) The article of Claim 1 wherein the drug present in the formulation is of low water solubility.
13. (original) The article of Claim 1 wherein the drug present in the formulation is selected from the group consisting of acetohexamide, acetylsalicylic acid, alclofenac, allopurinol, atropine, benzthiazide, carprofen, celecoxib, chlordiazepoxide, chlorpromazine, clonidine, codeine, codeine phosphate, codeine sulfate, deracoxib, diacerein, diclofenac, diltiazem, eplerenone, estradiol, etodolac, etoposide, etoricoxib, fenbufen, fenclofenac, fenprofen, fentiazac, flurbiprofen, griseofulvin, haloperidol, ibuprofen, indomethacin, indoprofen, ketoprofen, lorazepam, medroxyprogesterone acetate, megestrol, methoxsalen, methylprednisone, morphine, morphine sulfate, naproxen, nicergoline, nifedipine, niflumic, oxaprozin, oxazepam, oxyphenbutazone, paclitaxel, phenindione, phenobarbital, piroxicam, pirprofen, prednisolone, prednisone, procaine, progesterone, pyrimethamine, rofecoxib, sulfadiazine, sulfamerazine, sulfisoxazole, sulindac, suprofen, temazepam, tiaprofenic acid, tilomisol, tolmetic and valdecoxib.
14. (original) The article of Claim 1 wherein the drug present in the formulation is a steroidal drug.
15. (original) The article of Claim 14 wherein the steroidal drug is selected from the group consisting of clostebol, estradiol, exemestane, medroxyprogesterone,

PATENT/Docket No. PC27664A
Serial No. 10/644,516

methylprednisolone, testosterone and pharmaceutically acceptable esters and salts thereof.

16. (original) The article of Claim 14 wherein the steroidal drug is selected from the group consisting of estradiol cypionate, exemestane and medroxyprogesterone acetate.
17. (original) The article of Claim 14 wherein the steroidal drug is medroxyprogesterone acetate.
18. (original) The article of Claim 17 wherein the medroxyprogesterone acetate is present in an amount of about 10 to about 400 mg/ml.
19. (original) The article of Claim 17 wherein the medroxyprogesterone acetate is present in an amount of about 30 to about 300 mg/ml.
20. (original) The article of Claim 17 wherein the medroxyprogesterone acetate is present in an amount of about 50 to about 200 mg/ml.
21. (original) The article of Claim 17 wherein the formulation comprises:
 - (a) medroxyprogesterone acetate, 100–200 mg/ml;
 - (b) polyethylene glycol of molecular weight 3000–4000, 20–40 mg/ml;
 - (c) polysorbate 80, 2–4 mg/ml;
 - (d) sodium chloride, 6–12 mg/ml; and
 - (e) optionally at least one parenterally acceptable preservative, 0.1–5 mg/ml total.
22. (original) The article of Claim 17 wherein the formulation comprises:
 - (a) medroxyprogesterone acetate, about 150 mg/ml;
 - (b) polyethylene glycol of molecular weight about 3350, about 30 mg/ml;
 - (c) polysorbate 80, about 2.5 mg/ml;
 - (d) sodium chloride, about 9 mg/ml;
 - (e) methylparaben, about 1.5 mg/ml;
 - (f) propylparaben, about 0.15 mg/ml; and
 - (g) water for injection, *q.s.*
23. (original) The article of Claim 17 wherein the formulation comprises. in a volume

PATENT/Docket No. PC27664A
Serial No. 10/644,516

of about 0.65 ml:

- (a) medroxyprogesterone acetate, about 104 mg;
- (b) polyethylene glycol of molecular weight about 3350, about 18.7 mg;
- (c) polysorbate 80, about 1.95 mg;
- (d) sodium chloride, about 5.2 mg;
- (e) methylparaben, about 1.04 mg;
- (f) propylparaben, about 0.10 mg;
- (g) monobasic sodium phosphate monohydrate, about 0.45 mg;
- (h) dibasic sodium phosphate dodecahydrate, about 0.38 mg;
- (i) L-methionine, about 0.98 mg;
- (j) polyvinylpyrrolidone K17, about 3.25 mg; and
- (k) water for injection, *q.s.*